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Docket No. 64481/JPW/AJM/MML

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Isabelle Mansuy and Eric R. Kandel  
Serial No. : 10/091,714  
Filed : March 5, 2002  
For : CALCINEURIN-RELATED TRANSGENIC MAMMALS,  
COMPOSITIONS AND METHODS

1185 Avenue of the Americas  
New York, New York 10036  
July 11, 2002

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants request that the following disclosures be made of record in the above-identified application pursuant to 37 C.F.R. §1.97(b). These references are also listed on the Form PTO-1449 attached hereto as **Exhibit A**. Copies of these references are attached hereto as **Exhibits 1-34**, respectively.

1. U.S. Patent Application Publication No. 00/18207, published August 30, 2001, Kandel et al. (**Exhibit 1**);
2. U.S. Patent No. 5,567,724, issued October 22, 1996, Kelleher et al. (**Exhibit 2**);
3. U.S. Patent No. 5,720,936, issued February 24, 1998, Wadsworth et al. (**Exhibit 3**);
4. U.S. Patent No. 5,723,436, issued March 3, 1998, Huang et al. (**Exhibit 4**);

5. U.S. Patent No. 5,807,693, issued September 15, 1998, Scott et al. **(Exhibit 5)**;
6. U.S. Patent No. 6,323,391, issued November 27, 2001, Schlaepfer et al. **(Exhibit 6)**;
7. Abel, T., et al., "Memory suppressor genes: inhibitory constraints on the storage of long-term memory," *Science*, 279:338-341 (1998) **(Exhibit 7)**;
8. Bach, M.E., et al., "Age-related defects in spatial memory are correlated with defects in the late phase of hippocampal long-term potentiation *in vitro* and are attenuated by drugs that enhance the cAMP signaling pathway," *Proc. Natl. Acad. Sci. U.S.A.*, 96:5280-5285 (1999) **(Exhibit 8)**;
9. Buhot, M.-C., and Naili, S., "Changes in exploratory activity following stimulation of hippocampal 5-HT1A and 5-HT1B receptors in the rat," *Hippocampus*, 5:198-208 (1995) **(Exhibit 9)**;
10. Cassel, J.-C., et al., "Fimbria-fornix versus selective hippocampal lesions in rats: effects on locomotor activity and spatial learning and memory," *Neurobiol. Learn. Mem.*, 69:22-45 (1998) **(Exhibit 10)**;
11. Errington, M.L., et al., "Long-term potentiation in awake mutant mice," *Nature*, 387:666-667 (1997) **(Exhibit 11)**;

12. Gossen, M., et al., "Transcriptional activation by tetracyclines in mammalian cells," *Science*, 268:1766-1769 (1995) **(Exhibit 12)**;
13. Ikegami, S., et al., "A facilitatory effect on the induction of long-term potentiation in vivo by chronic administration of antisense oligodeoxy-nucleotides against catalytic subunits of calcineurin," *Brain Res. Mol. Brain Res.*, 41:183-191 (1996) **(Exhibit 13)**;
14. Ikegami, S., and Inokuehi, K. "Antisense DNA against calcineurin facilitates memory in contextual fear conditioning by lowering the threshold for hippocampal long-term potentiation induction," *Neuroscience*, 98:637-646 (2000) **(Exhibit 14)**;
15. Jerecic, J., et al., "Studies on conditional gene expression in the brain," *Ann. N.Y. Acad. Sci.*, 868:27-37 (1999) **(Exhibit 15)**;
16. Lisman, J. "The CaM kinase II hypothesis for the storage of synaptic memory," *Trends Neurosci.*, 17:406-412 (1994) **(Exhibit 16)**;
17. Lu, Y.-F., et al. "Calcineurin inhibitors, FK506 and cyclosporin A, suppress the NMDA receptor-mediated potentials and LTP, but not depotentiation in the rat hippocampus" *Brain Res.*, 729:142-146 (1996) **(Exhibit 17)**;

18. Lu, Y.M., et al., "Calcineurin mediated long-term depression of GABAergic inhibition underlies the long-lasting increase in the excitability of CA1 hippocampal pyramidal cells induced by LTP," *Neuron*, 26:197-205 (2000) **(Exhibit 18);**
19. Malleret, G., et al., "5-HT1B receptor knock-out mice exhibit increased exploratory activity and enhanced spatial memory performance in the Morris water maze," *J. Neurosci.*, 19:6157-6168 (1999) **(Exhibit 19);**
20. Malleret, G., et al., "Inducible and reversible enhancement of learning, memory, and long-term potentiation by genetic inhibition of calcineurin," *Cell*, 104:675-686 (2001) **(Exhibit 20);**
21. Mansuy, I.M., et al., "Restricted and regulated overexpression reveals calcineurin as a key component in the transition from short-term to long-term memory," *Cell*, 92:39-49 (1998) **(Exhibit 21);**
22. Mansuy, I.M., et al., "Inducible and reversible gene expression with the rtTA system for the study of memory," *Neuron*, 21:257-265 (1998) **(Exhibit 22);**
23. Morris, R.G.M., "Synaptic plasticity and learning: selective impairment of learning in rats and blockade of long-term potentiation in vivo by the N-methyl-D-aspartate receptor antagonist AP5", *J. Neurosci.*, 9:3040-3057 (1989) **(Exhibit 23);**

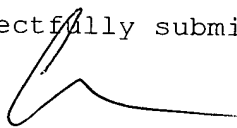
24. Mulkey, R.M., et al., "Involvement of a calcineurin/inhibitor-1 phosphatase cascade in hippocampal long-term depression," *Nature*, 369:486-488 (1994) **(Exhibit 24)**;
25. Parsons, J.N., et al., "Regulation of calcineurin phosphatase activity and interaction with the FK-506-FK-506 binding protein complex," *J. Biol. Chem.*, 269:19610-19616 (1994) **(Exhibit 25)**;
26. Perrino, B.A., et al., "Calcium regulation of calcineurin phosphatase activity by its B subunit and calmodulin. Role of the autoinhibitory domain," *J. Biol. Chem.*, 270:340-346 (1995) **(Exhibit 26)**;
27. Tang, Y.P., et al., "Genetic enhancement of learning and memory in mice," *Nature*, 407:63-69 (1999) **(Exhibit 27)**;
28. Tong, G., et al., "Synaptic desensitization of NMDA receptors by calcineurin," *Science*, 267:1510-1512 (1995) **(Exhibit 28)**;
29. Wang, J.-H. and Stelzer, A., "Inhibition of phosphatase 2B prevents expression of hippocampal long-term potentiation," *Neuroreport*, 5:2377-2380 (1994) **(Exhibit 29)**;
30. Wang, J.-H., and Kelly, P.T., "The balance between postsynaptic  $\text{Ca}^{2+}$ -dependent protein kinase and phosphatase activities controlling synaptic strength," *Learn. and Mem.*, 3:170-181 (1996) **(Exhibit 30)**;

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31. Wang, J.H., and Kelly, P.T. "Postsynaptic calcineurin activity downregulates synaptic transmission by weakening intracellular Ca<sup>2+</sup> signaling mechanisms in hippocampal CA1 neurons," *J. Neurosci*, 17:4600-4611 (1997) **(Exhibit 31)**;
32. Watanababe, Y., et al., "Identification in the calcineurin A subunit of the domain that binds the regulatory B subunit," *J. Biol. Chem.*, 270:456-460 (1995) **(Exhibit 32)**;
33. Winder, D.G., et al., "Genetic and pharmacological evidence for a novel, intermediate phase of long-term potentiation suppressed by calcineurin," *Cell*, 92:25-37 (1998) **(Exhibit 33)**; and
34. Zhuo, M., et al., "A selective role of calcineurin A $\alpha$  in synaptic depotentiation in hippocampus," *Proc. Natl. Acad. Sci. U.S.A.*, 96:4650-4655 (1999) **(Exhibit 34)**.

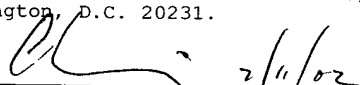
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

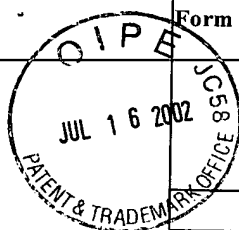


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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:  
Assistant Commissioner for Patents,  
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Alan J. Morrison  
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Atty. Docket No.

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Serial No.

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**INFORMATION DISCLOSURE CITATION**  
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**Applicants: Isabelle Mansuy and**  
**Eric R. Kandel**

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**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	0 0 1 8 2 0 7	08/30/2001	Kandel et al. (Exhibit 1);			
	5 5 6 7 7 2 4	10/22/1996	Kelleher et al. (Exhibit 2);			
	5 7 2 0 9 3 6	02/24/1998	Wadsworth et al. (Exhibit 3);			
	5 7 2 3 4 3 6	03/3/1998	Huang et al. (Exhibit 4);			
	5 8 0 7 6 9 3	09/15/1998	Scott et al. (Exhibit 5);			
	6 3 2 3 3 9 1	11/27/2001	Schlaepfer et al. (Exhibit 6);			

**FOREIGN PATENT DOCUMENTS**

Document Number	Date	Country	Class	Subclass	Translation
					Yes No

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

	Abel, T., et al., "Memory suppressor genes: inhibitory constraints on the storage of long-term memory," <i>Science</i> , 279:338-341 (1998) (Exhibit 7);
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**(Exhibit A)**

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